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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/653,406	09/01/2000	Jennifer L. West	RICE 100	7133

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EXAMINER	
DI NOLA BARON, LILIANA	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 10/03/2003

23

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/653,406	WEST ET AL.	
	Examiner	Art Unit	
	Liliana Di Nola-Baron	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *1-17,19 and 25-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18 and 20-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 September 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group III, claims 18 and 20-24, in Paper No. 22 is acknowledged. The traversal is on the ground(s) that examination of the claims of the entire application will not impose an undue burden. This is not found persuasive because the compositions of Group I require the presence of three different regions in the macromer, whereas the method of Group II requires a macromer comprising a NO carrying or producing region, and the methods of Group III requires the presence of one region in the macromer. Thus, the search to be conducted for Group I is different from the search for Group II or the search for Group III.

The requirement is still deemed proper and is therefore made FINAL. Accordingly, claims 18 and 20-24 will be examined in this Office action. Claims 1-17, 19 and 25-31 are withdrawn from consideration.

Specification

2. The preliminary amendment filed on November 27, 2000 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention.

The added material which is not supported by the original disclosure is as follows:

On page 4, lines 9-10, the phrase "which preferably include biodegradable regions" has been changed to "which may include biodegradable regions". This amendment represents a departure from the specification as originally filed, since, according to the amendment, the presence of biodegradable regions, originally contemplated as preferable, would no longer be required in the macromer of the invention.

On page 10, line 8, the phrase " The polymerizable regions are preferably polymerizable by photoinitiation" has been changed to "The polymerizable regions may be polymerizable by photoinitiation". This amendment represents a departure from the specification as originally filed, since, according to the amendment, polymerization of macromer regions by photoinitiation, originally contemplated as preferable, would no longer be required in the invention.

Applicant is required to cancel the new matter in the reply to this Office Action.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 20-23 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 20-23 of copending Application No. 10/129418. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are drawn to a method of treatment comprising administering a macromer composition comprising a NO carrying region or NO modulating compound.

Claim 20 in the instant application differs from claim 20 in the copending application in the following ways:

a. It includes the limitation that the NO or NO modulating compound is released from the macromer composition following polymerization in situ under physiological conditions. Copending claim 20 recites the limitation that the NO or NO modulating compound is released from the macromer composition, however, said release is not limited to after polymerization in situ under physiological conditions. Thus, copending claim 20 is broader than instant claim 20. The NO release recited in claim 20 of the copending application may however take place after polymerization in situ under physiological conditions, since nothing prevents said release from occurring. In fact, Applicant's specification in copending application teaches that the polymeric materials of the invention produce NO and polymerize in situ (See p. 9, lines 14-16). Furthermore, there is nothing physically different between the compositions administered in the method claimed in the instant application and the composition administered in the method

claimed in the copending application (See b. below), that would justify differences in NO releasing properties.

b. The macromers of instant claim 20 comprise regions selected from the group consisting of water-soluble regions, tissue adhesive regions and polymerizable end group regions, whereas the macromer claimed in claim 20 of the copending application has regions selected from the group consisting of a water-soluble region, a cell adhesion ligand and a polymerizable region. Applicant's specification of the instant application teaches that ligands, such as RGD peptides and lectines, which bind to carbohydrate molecules on cells, can also be bound to the polymer to increase tissue adhesiveness (See p. 7, lines 3-7). Additionally, Applicant's specification in the copending application teaches that cell adhesion peptide sequences are also referred to as cell adhesion ligands (See p. 10, lines 24-30) and ligands are contemplated by Applicant as tissue adhesive regions (See specification in copending application, p. 11, lines 21-26). Thus, tissue adhesive regions and cell adhesion ligands are considered synonymous terms. With regard to the polymerizable regions, claim 20 in the copending application recites the limitation "a polymerizable region" and not the limitation "polymerizable end group regions" as recited in instant claim 20. Thus, copending claim 20 is broader than instant claim 20. Applicant's specification in the copending application teaches that polymerizable regions can be attached to water-soluble regions, which are attached to the core of the macromer (See p. 14, lines 14-18), thus the specification of the copending application provides support for polymerizable end group regions, that would render obvious the subject matter claimed in instant claim 20.

Instant claim 23 and copending claim 23 present idiomatic differences, however, both claims are directed to a macromer adhered to tissue or coated onto tissue.

Although the scope of the copending claims is broader than the scope of the instant claims, the two sets of claims are largely coextensive.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 18 and 20-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roth et al. (U.S. Patent 5,879,713) in view of Trescony et al. (U.S. Patent 5,994,444).

Roth et al. discloses biodegradable macromers for targeted delivery of bioactive agents, which can be rapidly gelled while in contact with aqueous tissue fluids, and teaches that release of the bioactive material is prior to degradation or by diffusion from the polymer as it degrades (See col. 4, line 55 to col. 5, line 39). Roth et al. teaches that the macromers of the invention may be

polymerized in situ to serve as carriers for living cells or biologically active material, surgical adhesives or coatings for the treatment of restenosis (See col. 5, lines 40-52). Roth et al. teaches that the macromers of the invention include a biodegradable region, a water-soluble region and at least two photopolymerizable end group regions (See col. 5, line 53 to col. 6, line 67) and can be administered directly or indirectly (See col. 10, line 65 to col. 11, line 11).

Thus, with respect to claims 18, 20 and 21, Roth et al. provides methods for the controlled delivery of bioactive agents and methods of treatment, comprising administering a macromer composition comprising a biodegradable region, a water-soluble region and polymerizable end group regions, which is polymerized in situ, and teaches that the release of bioactive agents occurs during degradation of the polymer or by diffusion from the polymer. Thus the release of the bioactive agent occurs after polymerization in situ, as claimed by Applicant. The water-soluble regions disclosed by the patent are tissue adhesives, as claimed by Applicant. Roth et al. is deficient in the sense, that the patent does not specify the biologically active agents, and specifically NO modulating compounds, which may be trapped and released from the macromers of the invention.

With regard to claims 22 and 24, Roth et al. provides the teachings that the compositions of the invention may be used to treat restenosis (See col. 5, lines 48-52) and may be applied to a tissue lumen or hollow space, which may occur as a result of surgery, percutaneous techniques, trauma or disease (See col. 11, lines 41-51).

Regarding claim 23, Roth et al. teaches that the polymeric material of the invention may be formed into a coating or sealing for the treatment of biological or clinical situations (See col. 11, lines 50-65).

Trescony et al. provides a biocompatible biodegradable polymeric material capable of releasing nitric oxide at an intended site in vivo and discloses a nitric oxide donor embedded in a polymer matrix for the treatment of thrombogenesis (See col. 2, lines 5-49 and col. 3, lines 1-67).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the methods disclosed by Roth et al., by embedding a nitric oxide donor in the macromer of the invention, as taught by Trescony et al., to treat diseases related to NO conditions. The expected result would have been a successful method for the controlled release of therapeutic agents and a successful method of treatment. Because of the teachings of Roth et al., that the macromers of the invention may be used for the controlled release of active agents and for the treatment of diseases, including restenosis, and the teachings of Trescony et al., that nitric oxide may be released from biodegradable polymers entrapping nitric oxide donors for the local treatment of NO-related conditions, one of ordinary skill in the art would have a reasonable expectation that the methods claimed in the instant application would be successful at providing treatment of NO-related diseases. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

7. Applicant's arguments, filed on April 29, 2003, with respect to the rejection of claims 1-23 under 35 U.S.C. 103(a) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground of rejection is made as explained above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liliana Di Nola-Baron whose telephone number is 703-308-8318. The examiner can normally be reached on Monday through Thursday, 5:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 308-1234/ 1235.

Liliana Di Nola Baron

October 1, 2003

Liliana Di Nola-Baron
Patent Examiner
Art Unit 1615